



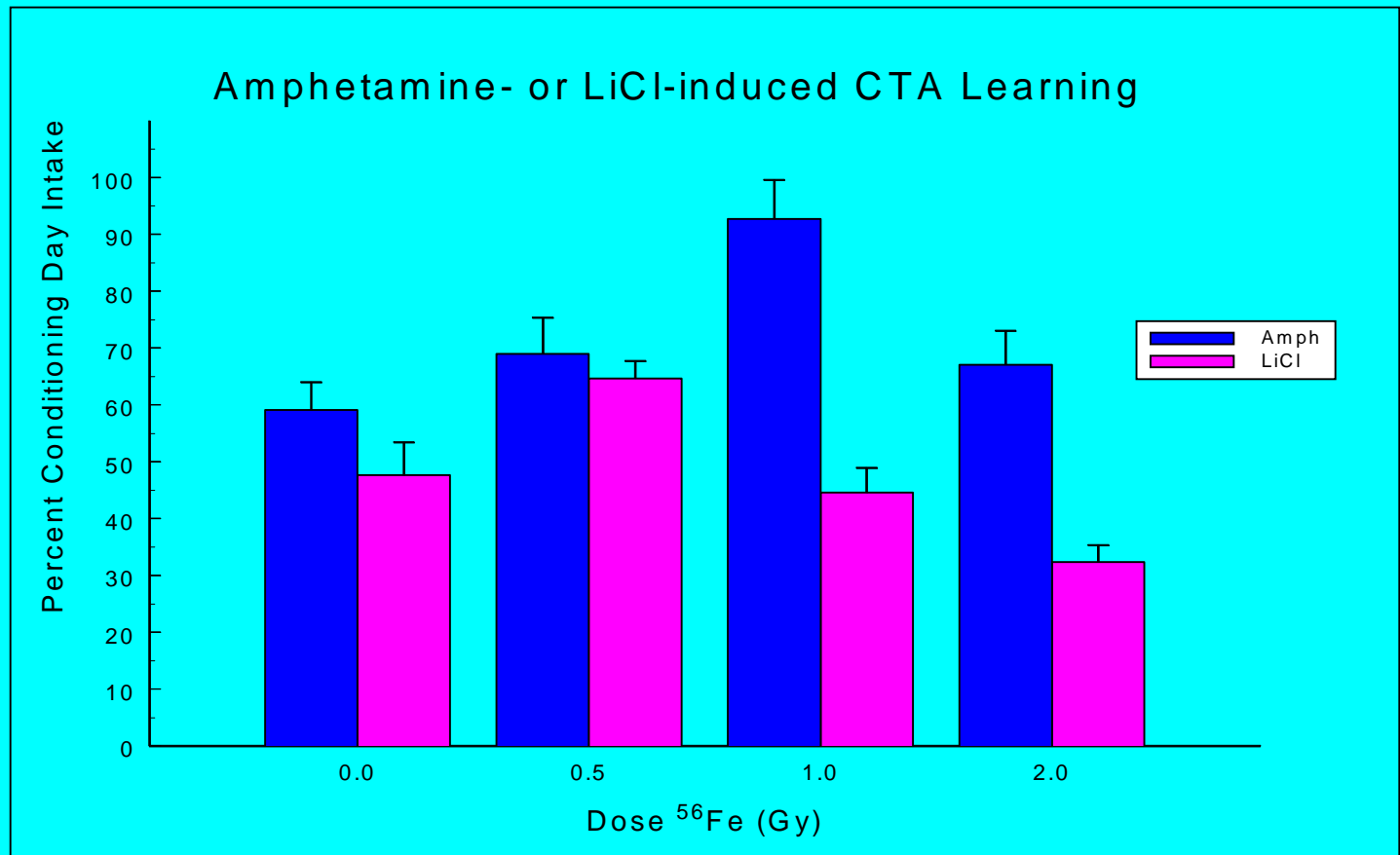
Neurochemical and Behavioral Effects of Exposure to Heavy Particles

Bernard M. Rabin

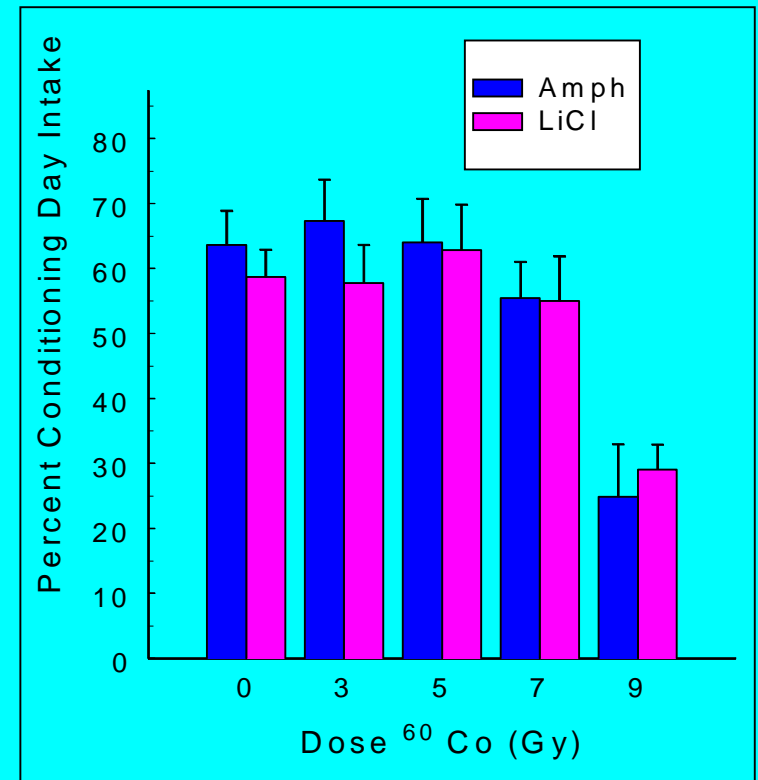
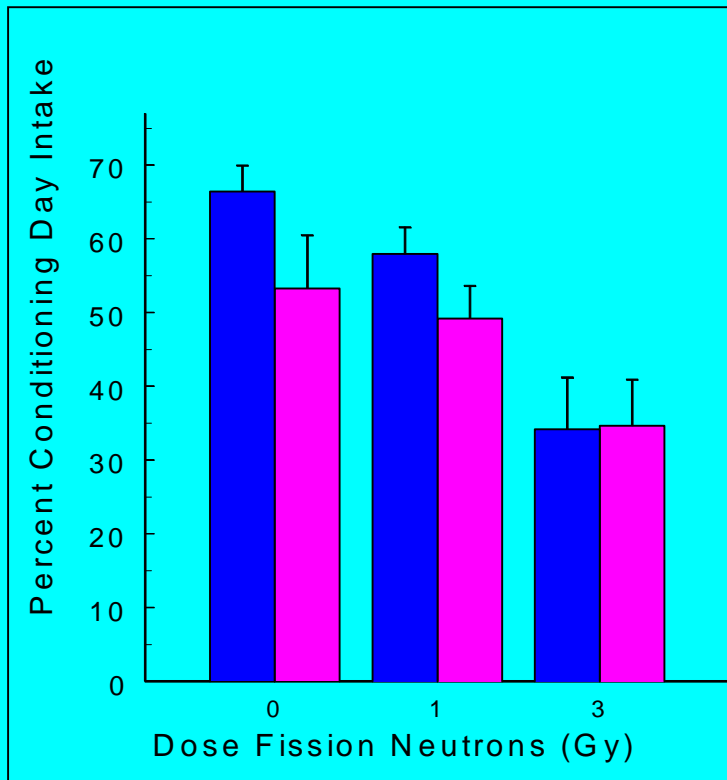
James A. Joseph

Barbara Shukitt-Hale

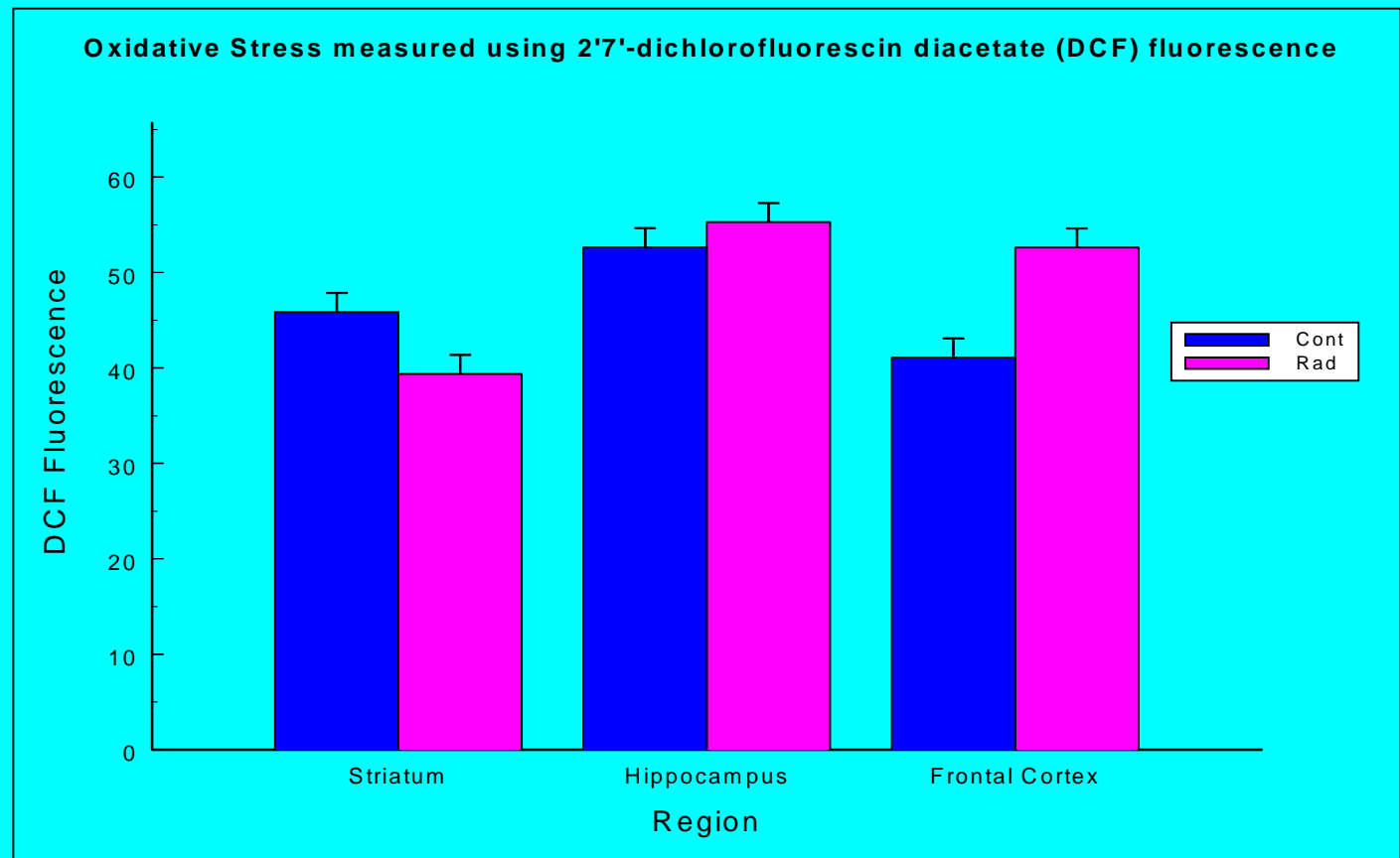
Exposure to 1 GeV/n ^{56}Fe Particles Disrupts a Dopamine-Mediated Behavior



Exposure to Fission Neutrons or ^{60}Co Gamma Rays Does Not Affect Dopamine-Mediated Behavior



Oxidative Stress Following Exposure to ^{56}Fe Particles

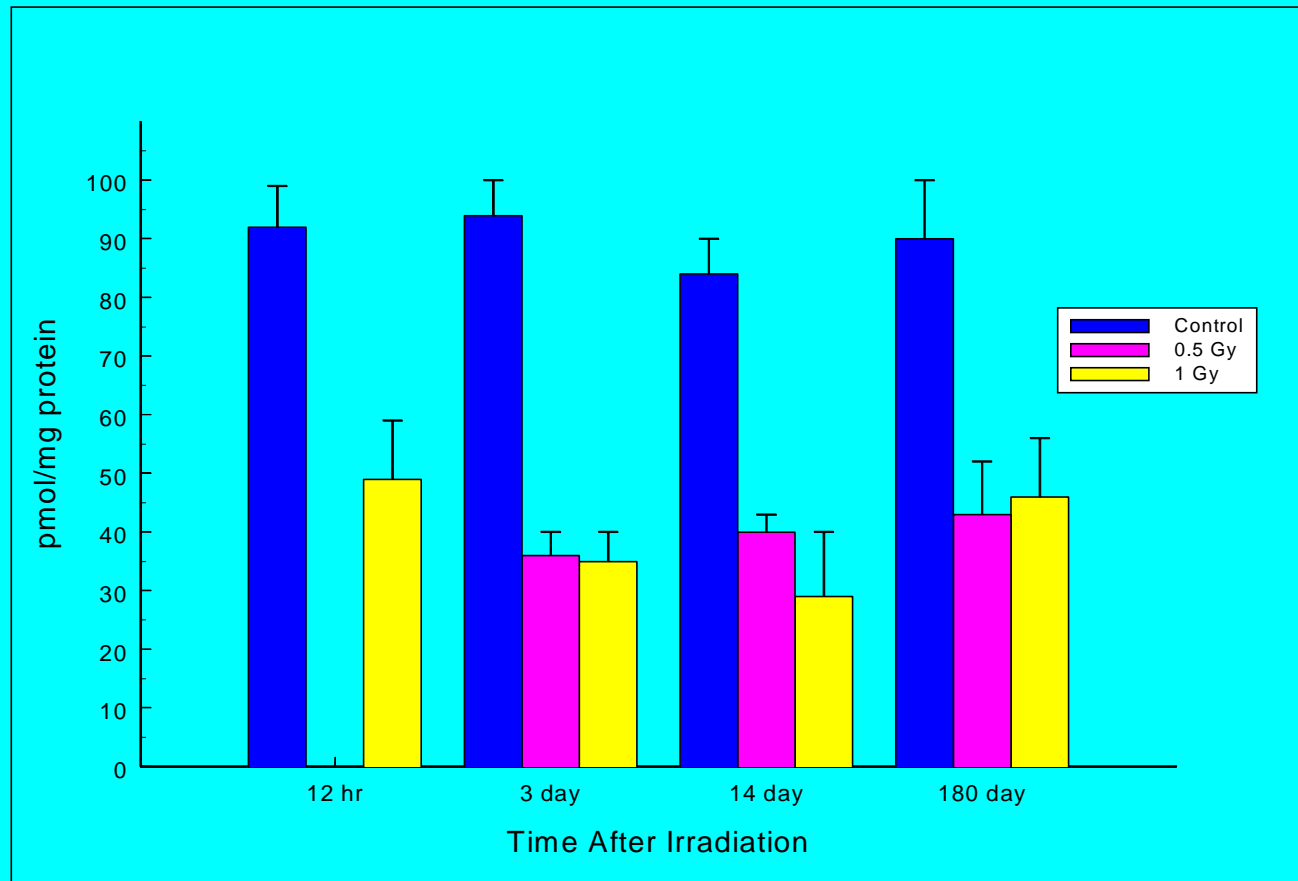




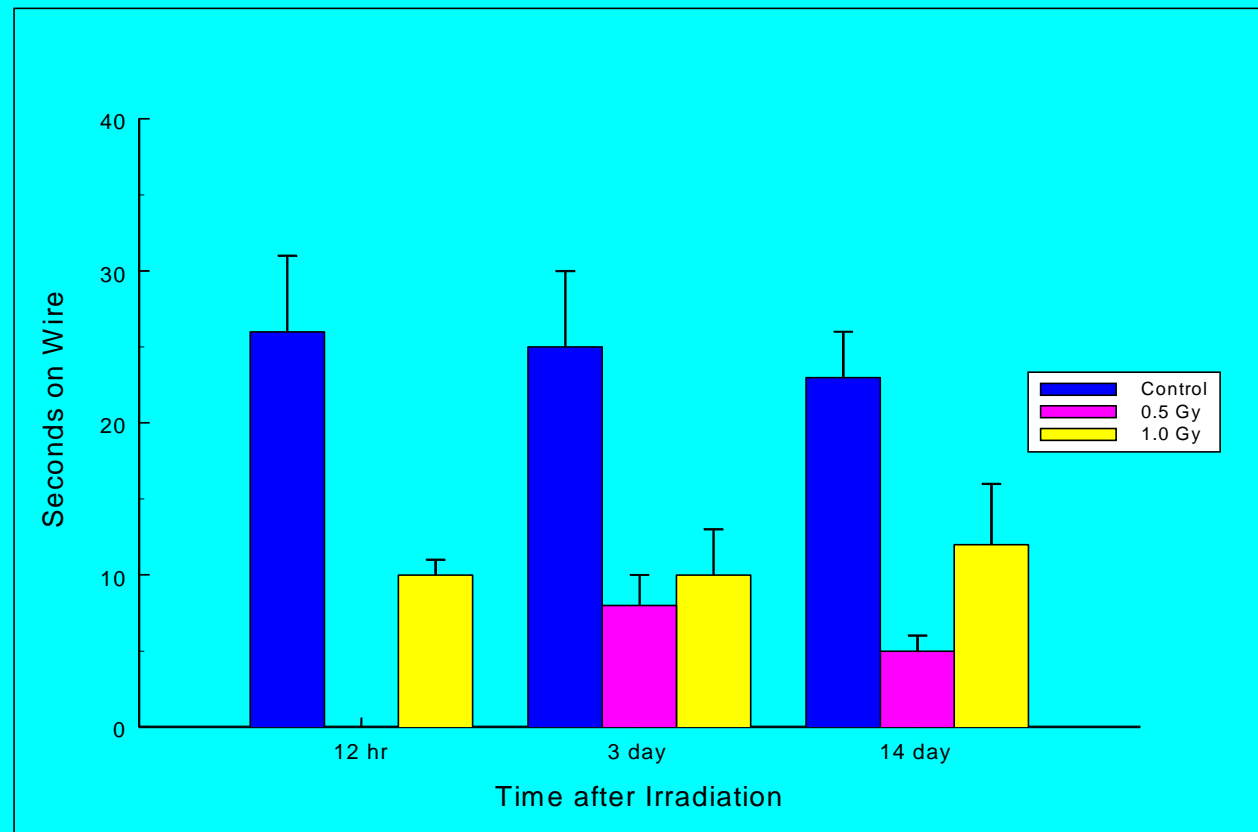
Oxidative Stress

- Greater production than scavenging of free radicals
- Interactions between free radicals and dopamine in the CNS
 - Oxidation of dopamine by monoamine oxidase can produce hydroxyl radicals
- Effects of oxidative stress include:
 - Aging
 - Neurodegenerative disorders
 - Parkinson's Disease
 - Alzheimer's Disease

Peak Dopamine Release from Striatal Tissue



Time on wire following exposure to ^{56}Fe particles



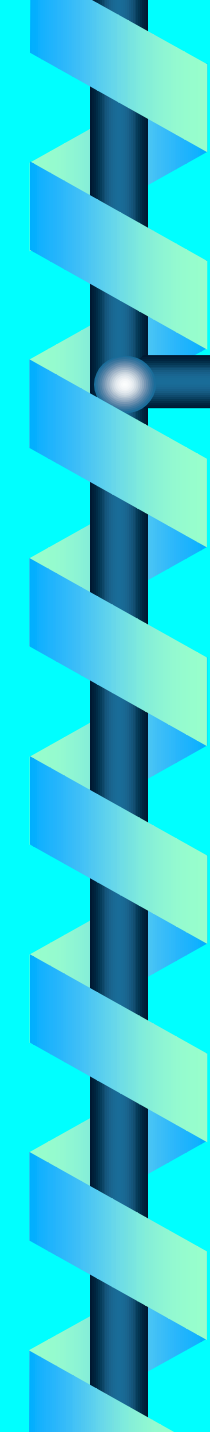


Health Effects of Exposure to ^{56}Fe Particles: Accelerated Aging

- Changes in dopaminergic function and motor performance that characterize old rats
- Changes are immediate and permanent
- Functional changes in dopaminergic system
 - Changes in signal transduction at the receptor\g-protein interface
 - Deficits in muscarinic receptor sensitivity
 - Possible changes in membrane structure

Health Effects of Exposure to ^{56}Fe Particles: Parkinson's Disease

- Animal models for Parkinson's disease
 - Dopamine loss produced by 6-OHDA
 - Dopamine loss produced by ^{56}Fe exposure?
- Dopamine-Mediated Deficits
 - Motor
 - Akinesia, Rigidity, Tremor
 - Cognitive
 - Visuospatial performance
 - Skilled motor control



Behavioral Effects of Exposure to Heavy Particles: Cognitive Deficits

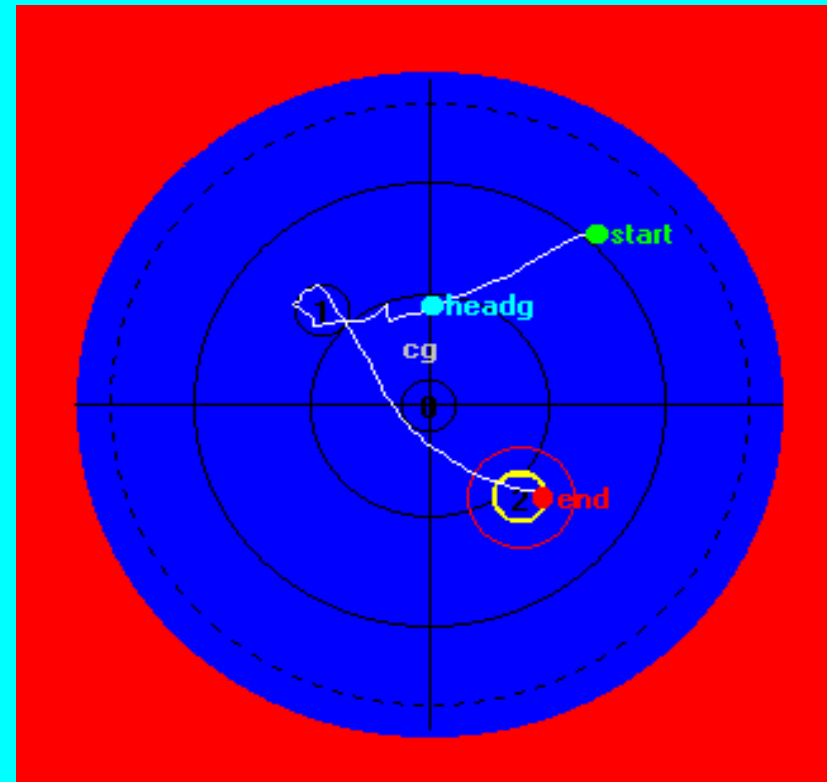
- Aging: spatial learning and memory
 - Morris water maze
- Dopamine: reinforcement mechanisms
 - Conditioned place preference

Morris Water Maze – Performance on Trial 2, Day 4 Reversal

RADIATED

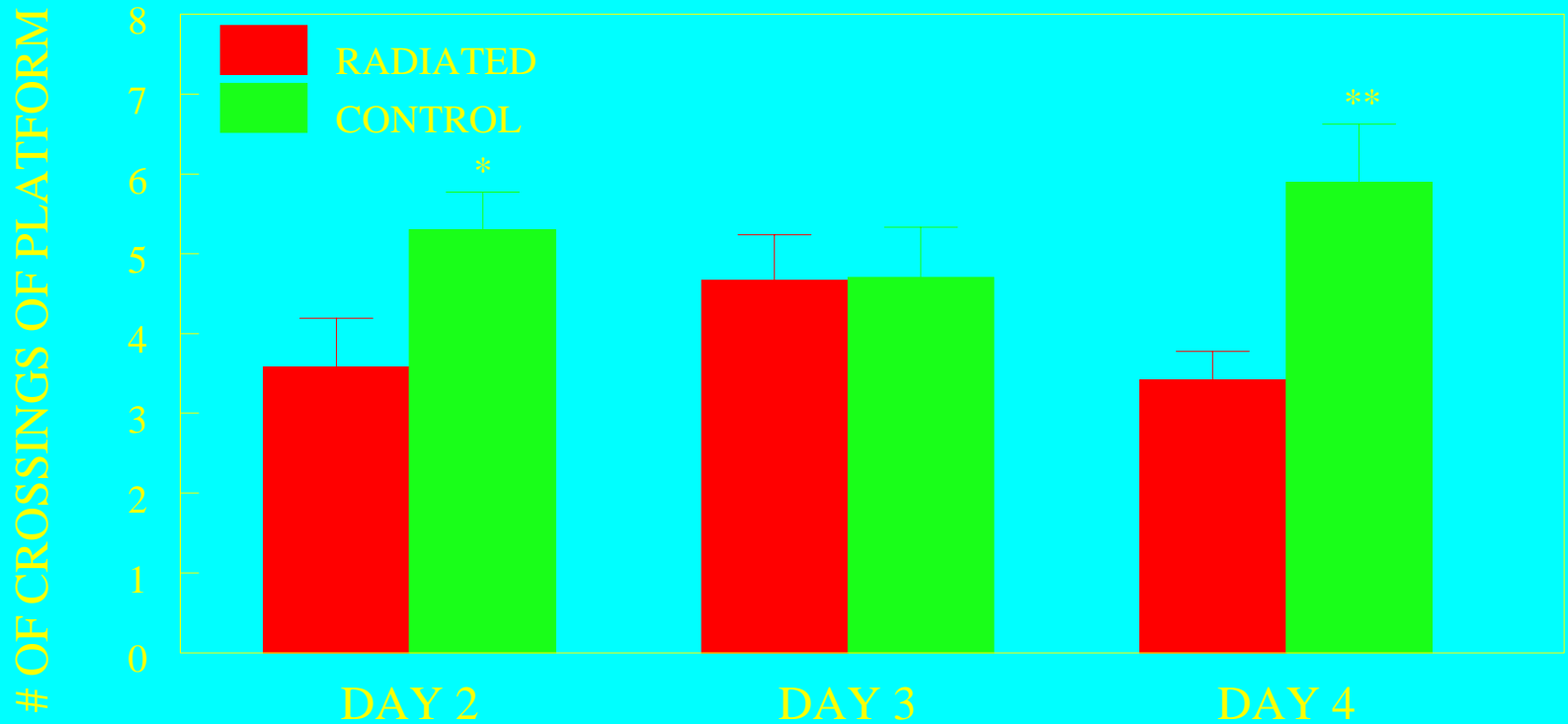


CONTROL

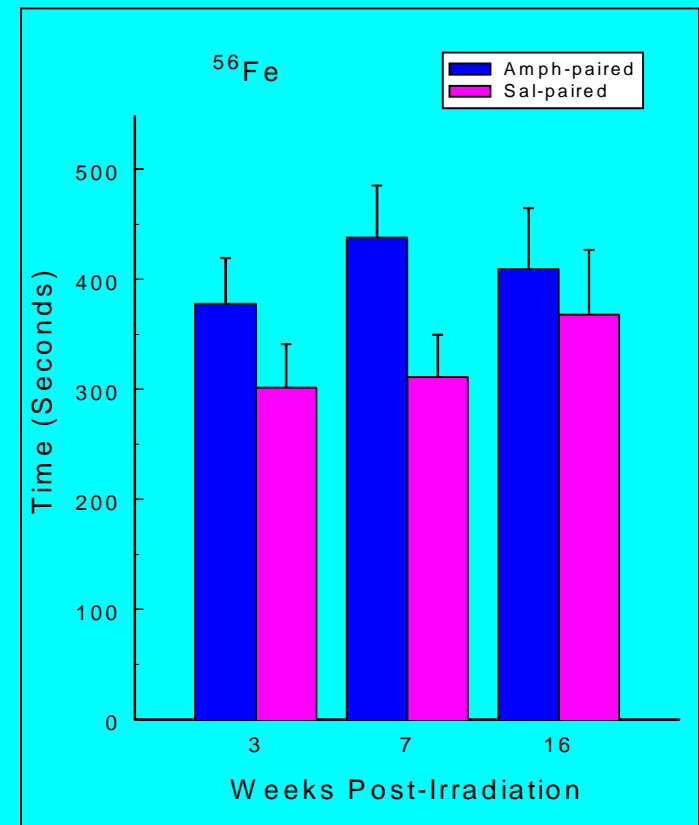
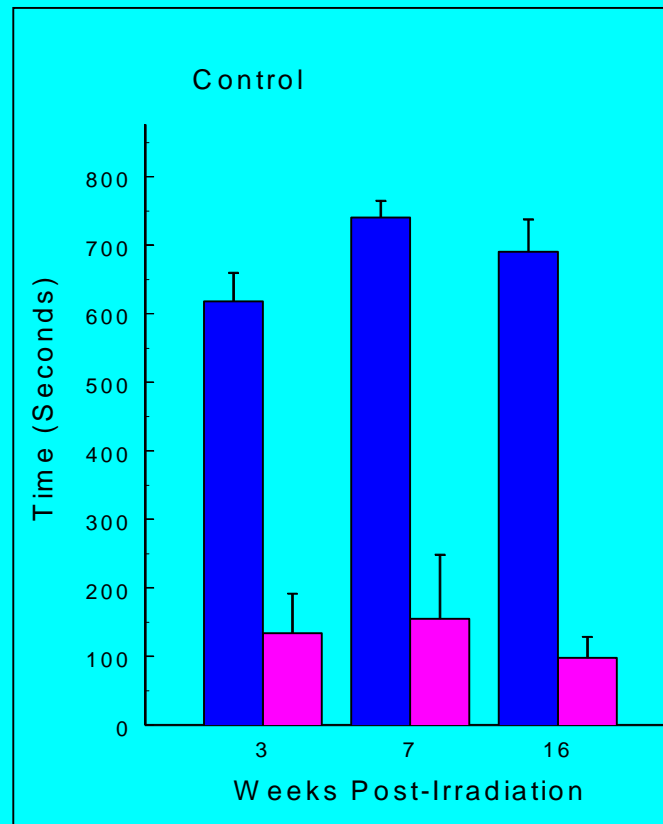


Exposure to 1.5 Gy of ^{56}Fe particles disrupts spatial learning and memory determined using the Morris Water Maze

PROBE TRIALS



Exposure to 1.0 Gy of ^{56}Fe particles disrupts dopamine-mediated reinforcement mechanisms using the conditioned place preference





Health and Behavioral Effects of Exposure to ^{56}Fe Particles: Prevention

- Reduce Oxidative Stress
 - Free Radical Scavengers/Antioxidants
 - Vitamin E; Glutathione; Pergolide; Ethanol
 - Dietary Antioxidants
 - Blueberry; Strawberry
- Reduce Effects on Dopaminergic Neurons
 - Estrogen